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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/646,391	08/21/2003	Martin Gleave	UBC.P-035	9734

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EXAMINER
BOWMAN, AMY HUDSON

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/08/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/646,391	GLEAVE ET AL.	
	Examiner	Art Unit	
	Amy H. Bowman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *24 February 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13* is/are pending in the application.

4a) Of the above claim(s) *11-13* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *21 August 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/20/2004*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse of SEQ ID NO: 4 and the corresponding translation initiation site, directed to claims 1-10, in the reply filed on 2/24/2005 is acknowledged.

Applicant states that they do not object to a requirement for election of species, but that they do disagree with any characterization of these claims as improper. In particular, applicant argues that these claims are dependent claims, and each of the members in the Markush group shares the common property of being useful in the method as claimed.

It is noted that the requirement for restriction/election was not a species election, but rather an improper Markush. Further, claim dependency does not determine unity of invention. As explained in the official action mailed on 2/4/2005, each of the sequences are considered to be unrelated, since each sequence is structurally and functionally independent and do not share a common core. As such the Markush/genus of sequences in claims 6, 7, 9, 10 and 12 are not considered to constitute proper genus, and therefore are subject to restriction. Furthermore, a search of more than one of the sequences claimed in claims 6, 7, 9, 10 and 12 presents an undue burden on the Patent and Trademark Office due to the complex nature of the search and corresponding examination of more than one of the claimed sequences.

The requirement for restriction is still deemed proper and is therefore made FINAL.

Claims 11-13 are withdrawn as being drawn to non-elected inventions.

Claim Objections

Claims 3, 5, 6 and 9 are objected to because of the following informalities:

Claim 3 is drawn to an antisense oligo that spans either the translation initiation site or the termination site. Since applicant has elected the translation initiation site, the claim reads on non-elected subject matter.

It seems that applicant has either inadvertently omitted a paren in claim 5, or inadvertently inserted an extra paren in 2'-O-(2-methoxyethyl).

Claims 6 and 9 are drawn to SEQ ID NOS: 2 to 19. Since applicant has elected SEQ ID NO:4, claims 6 and 9 read on non-elected subject matter. If claims 6 and 9 are amended to read specifically on SEQ ID NO: 4, as elected, these claims would be substantial duplicates of claims 7 and 10, respectively.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 1-10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for reducing the effective amount of clusterin in melanoma cells *in vitro* and *in vivo* in mouse cells in mice via antisense oligonucleotide technology, does not reasonably provide enablement for the *in vivo* inhibition of clusterin in any organism via antisense oligonucleotide technology or for the treatment

of melanoma. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. Although the specification is enabling for inhibition of clusterin expression *in vitro*, it does not reasonably provide enablement for the inhibition of such cells *in vivo* or the treatment of an animal.

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide spans the translation initiation site and contains various modifications to the sugar or backbone, and wherein the antisense oligonucleotide consists essentially of SEQ ID NO: 4. The instant claims encompass *in vivo* effects.

The specification teaches antisense oligonucleotides directed against normal human melanocytes and human melanoma cell lines *in vitro* (page 8). The antisense inhibitor led to a dose dependent down-regulation of clusterin compared to the control.

The prior art teaches antisense oligonucleotide inhibition of clusterin in mice *in vivo*. For example, Gleave et al. (WO 00/49937) teach experiments comprising the intraperitoneal treatment of test mice with antisense oligonucleotides to TRPM-2, which is another name for Clusterin (page 6). Further, Gleave et al. used a tumor model, wherein the instant invention is drawn to melanoma.

Although applicant and/or the prior art have shown *in vitro* inhibition of clusterin, as well as the *in vivo* inhibition of mouse clusterin, the specification is not enabled for

the treatment of melanoma, particularly in a human. Inducing such symptoms in a mouse does not necessarily correlate to treating an actual diagnosed disorder, especially in a human. The specification as filed does not teach that because of administration of an antisense compound targeted to clusterin, treatment of conditions and diseases associated with clusterin expression *in vivo* results.

There is no guidance in the specification as filed that teaches how to target the claimed antisense compound to human cells or tissues *in vivo*, inhibit the expression of clusterin *in vivo*, and further provide treatment for melanoma. Although the specification discloses inhibition of clusterin mRNA *in vitro* by administration of antisense compound, such a disclosure would not be considered enabling since the state of antisense-mediated gene inhibition is highly unpredictable.

The following factors have been considered in the analysis of enablement: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the level of one of ordinary skill, (5) the level of predictability in the art, (6) the amount of direction provided by the inventor, (7) the existence of working examples, (8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

The breadth of claims 1-10 encompass methods of treating a broad range of melanomas in different tissues by use of an antisense targeted to a clusterin gene *in vivo*. Although the specification teaches inhibition of clusterin mRNA *in vitro* after treatment with an antisense compound, this guidance is not sufficient to resolve the

known unpredictability in the art associated with appropriate *in vivo* delivery and treatment effects provided by the instantly claimed methods.

The references cited herein illustrate the state of the art for therapeutic *in vivo* applications using antisense compounds. Branch stresses that "because it is very difficult to predict what portions of an RNA molecule will be accessible in vivo, effective antisense molecules must be found empirically by screening a large number of candidates for their ability to act inside cells" (TIB 23: 45-50 1998). Green *et al.* states that "[i]t is clear from the evolution of antisense technology from a laboratory research tool into a mechanism for designing active and effective drugs is far from complete. Although there is little doubt that systemically administered antisense [oligonucleotides] can inhibit the expression of specific genes in patients, the effectiveness of such therapy in modifying the course of a particular illness has not yet been established. In addition, toxicity in humans appears more problematic than might be predicted based on preclinical studies in rodents. Clearly, additional work must be done to unravel the complex problems associated with drug delivery, mRNA targeting and aptameric, nonantisense effects" (Antisense Therapy in Human Disease; Vol. 191, No. 1 2000, pg 103 column 2).

The problems with efficient delivery of antisense oligonucleotides to cells has been addressed by Jen *et al.*, who states that "[o]ne of the major limitations for the therapeutic use of AS-ODNS ...is the problem of delivery....presently, some success has been achieved in tissue culture, but efficient delivery for *in vivo* animal studies remains questionable (Stem Cells 2000; 18:307-319 pg 315 column 2)." Jen *et al.*

concludes that "[g]iven the state of the art, it is perhaps not surprising that effective and efficient clinical translation of the antisense strategy has proven elusive (see p 315, second column)."

As outlined above, it is well known that there is a high level of unpredictability in the antisense art for therapeutic *in vivo* applications. The scope of the claims in view of the specification as filed together do not reconcile the unpredictability in the art to enable one of skill in the art to make and/or use the claimed invention, namely treatment of melanoma by administration of an antisense compound targeted to a gene encoding clusterin.

While one skilled in the art may be able to find an antisense oligonucleotide targeted to a gene encoding clusterin and demonstrate inhibition of clusterin in cells *in vitro* after treatment with the antisense oligonucleotide, the specification as filed does not teach how to administer any antisense oligonucleotide to treat melanoma and further to treat by administration of the antisense compound intravenously, intraperitoneally, subcutaneously or orally, as disclosed in the specification, page 4.

Crooke (Antisense Research and Application, Chapter 1, Springer-Verlag, New York. 1998) supports the difficulties of extrapolating from in vitro experiments and states on p. 3, paragraph 2, "extrapolations from *in vitro* uptake studies to predictions about *in vivo* pharmacokinetic behavior are entirely inappropriate and, in fact, there are now several lines of evidence in animals and man [that] demonstrate that, even after careful consideration of all *in vitro* uptake data, one cannot predict *in vivo* pharmacokinetics of the compounds based on *in vitro* studies [references omitted]."

Furthermore, the prior art discloses a mouse model of inducing melanoma symptoms and inhibiting clusterin expression, but does not demonstrate treatment of melanoma, particularly in a human. Such a disclosure would not be considered enabling for treatment of melanoma because treatment is recognized as unpredictable in the art.

In view of the unpredictability in the art of antisense-based therapy, as outlined above, the specification as filed does not provide adequate guidance that would show how one skilled in the art would practice the claimed invention without undue experimentation.

Given the teachings of the specification as discussed above, one skilled in the art would not know *a priori* whether introduction of antisense oligonucleotides *in vivo* by the broadly disclosed methodologies of the instantly claimed invention, would result in successful inhibition of expression of a target gene resulting in treatment of melanoma. To practice the claimed invention, one of skill in the art would have to *de novo* determine; the stability of the antisense molecule *in vivo*, delivery of the antisense molecule to the whole organism, specificity to the target tissue *in vivo*, dosage and toxicity *in vivo*, and entry of the molecule into the cell *in vivo* and the effective action therein. Without further guidance, one of skill in the art would have to practice a substantial amount of trial and error experimentation, an amount considered undue and not routine, to practice the instantly claimed invention.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-5 are rejected under 35 U.S.C. 102(a) as being anticipated by Monia et al. (U.S. 2004/0053874).

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide spans the translation initiation site and contains various modifications to the sugar or backbone.

Monia et al. teach a method of treating an animal having a disease or condition associated with clusterin comprising administering to said animal a therapeutically effective amount of an antisense compound targeted to a nucleic acid molecule encoding clusterin, wherein said compound inhibits the expression of clusterin. The method taught by Monia et al. is considered to be as enabled as applicant's instant specification. Monia et al. teach an antisense oligonucleotide that spans the translation initiation site (see table 1). Additionally, Monia et al. teaches modifications to the antisense oligos including phosphorothioate linkages and 2'-O-methoxyethyl sugar

moieties to enhance stability (see pages 4 and 5). The method taught by Monia et al. is considered to be as enabled as applicants instant specification.

Therefore, the invention of claims 1-5 is anticipated by Monia et al.

Claims 1-5, 9 and 10 are rejected under 35 U.S.C. 102(b) as being anticipated by Gleave et al. (WO 00/49937, published 8/31/00).

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide spans the translation initiation site and contains various modifications to the sugar or backbone, and wherein the antisense oligonucleotide consists essentially of SEQ ID NO: 4. Additionally, the instant oligonucleotides are taught to be administered by intravenous, intraperitoneal, subcutaneous, oral routes or direct local tumor injection.

Gleave et al. teach a method for treating cancer, particularly prostate cancer, in a mammalian subject comprising the administration of an antisense oligonucleotide effective to inhibit expression of TRPM-2 (another name for clusterin) in tumor cells. The method taught by Gleave et al. is considered to be as enabled as applicant's instant specification. The antisense oligonucleotide taught by Gleave et al. spans the translation initiation site and is the same sequence as SEQ ID NO: 4 being instantly claimed (see SEQ ID NO:4 of Gleave et al.). Additionally, Gleave et al. teach

phosphorothioate and methoxyethyl modification of the antisense oligonucleotide to increase the stability of the oligonucleotide (see page 8). As stated in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property. Since the antisense sequence taught by Gleave et al. is the same sequence as instantly claimed, is taught to treat cancers, and can be administered in the same way as the instantly claimed antisense oligonucleotide (see example 1), the prior art antisense oligonucleotide would then be considered to have the inherent property of treating melanoma as well, as instantly claimed. Therefore, the invention of claims 1-5, 9 and 10 is anticipated by Gleave et al.

Claims 1-5, 9 and 10 are rejected under 35 U.S.C. 102(a) as being anticipated by Gleave. (US 2002/0128220 A1).

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide spans the translation initiation site and contains various modifications to the sugar or backbone, and wherein the antisense oligonucleotide consists essentially of SEQ ID NO: 4. Additionally, the instant oligonucleotides are taught to be administered by intravenous, intraperitoneal, subcutaneous, oral routes or direct local tumor injection.

Gleave teaches a method for treating cancer, particularly prostate cancer, in a mammalian subject comprising the administration of an antisense oligonucleotide effective to inhibit expression of TRPM-2 (another name for clusterin) in tumor cells. The method taught by Gleave is considered to be as enabled as applicant's instant specification. The antisense oligonucleotide taught by Gleave spans the translation initiation site and is the same sequence as SEQ ID NO: 4 being instantly claimed (see SEQ ID NO: 4 of Gleave). Additionally, Gleave teach phosphorothioate and 2'-O-(2-methoxyethyl) modification of the antisense oligonucleotide to increase the stability of the oligonucleotide. As stated in the MPEP (see MPEP 2112), something that is old does not become patentable upon the discovery of a new property. Since the antisense sequence taught by Gleave is the same sequence as instantly claimed, is taught to treat cancers, and can be administered in the same way as the instantly claimed antisense oligonucleotide (see example 1), the prior art antisense oligonucleotide would then be considered to have the inherent property of treating melanoma as well, as instantly claimed. Therefore, the invention of claims 1-4, 9 and 10 is anticipated by Gleave.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1-10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Gleave et al. (WO 00/49937), in view of Baracchini et al. (U.S. 5,801,154).

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide spans the translation initiation site and contains various modifications to the sugar or backbone, and wherein the antisense oligonucleotide consists essentially of SEQ ID NO: 4.

Gleave et al. teach a method for treating cancer in a mammalian subject comprising the administration of an antisense oligonucleotide effective to inhibit expression of TRPM-2 (another name for clusterin) in tumor cells. The antisense oligonucleotide taught by Gleave et al. spans the translation initiation site and is the same sequence as SEQ ID NO: 4 being instantly claimed (see SEQ ID NO:4 of Gleave et al.).

Gleave et al. do not teach modifications to the sugar or backbone of the antisense oligonucleotide.

Baracchini et al. teach that preferred antisense oligonucleotides are modified in their sugar, backbone linkage and nucleobase composition (col. 6). Baracchini et al. teach that such modifications are desirable in antisense oligos because these modifications have beneficial properties such as enhanced cellular uptake, enhanced affinity for nucleic acid targets and increased stability in the presence of nucleases.

Baracchini et al. provide specific embodiments of such modifications at columns 6-8 and in Example 1. These specific examples taught by Baracchini et al include the presently claimed phosphorothioate linkages, 2'-O-methoxyethyl sugars and chimeric oligonucleotides. Tables 1-4 show the successful design and use of modified oligonucleotides in cells.

It would have been obvious to one of ordinary skill to modify the antisense oligonucleotide taught by Gleave et al. with phosphorothioate linkages and 2'-O-methoxyethyl modifications as taught by Baracchini et al. One would have been motivated to incorporate modifications as taught by Baracchini et al. into said antisense oligonucleotide with the motivation of increasing an antisense compound's cellular uptake, target affinity and resistance to degradation, as taught by Baracchini et al.

Finally, one would have a reasonable expectation of success to incorporate such modifications because the modifications were known in the art to increase an antisense oligonucleotides cellular uptake, target affinity and resistance to degradation, as taught by Baracchini et al., which are all desirable properties for an antisense oligonucleotide.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Double Patenting Rejection

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11

F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1, 2, 9 and 10 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-3 of copending application no. 10/828,394, which has a common inventor. Although the conflicting claims are not identical, they are not patentably distinct from each other because they contain methods with overlapping scope.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

The instant invention is drawn to a method for treating melanoma in a mammalian subject, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the melanoma cells. The antisense oligodeoxynucleotide consists essentially of SEQ ID NO: 4.

Application '394 claims a method for treating a cancerous angiogenesis-related disease, comprising the step of administering to the subject a therapeutic agent, wherein said therapeutic agent is an antisense oligodeoxynucleotide, effective to reduce the effective amount of clusterin in the individual. The human clusterin

sequences taught by application '394 is SEQ ID NO: 1 (see claim 2), which is the same human clustering sequence instantly disclosed (instant SEQ ID NO: 1). The antisense oligodeoxynucleotide claimed by application '394 consists essentially of SEQ ID NOS: 2-15. SEQ ID NO: 4 of application '394 is the same as instantly claimed SEQ ID NO: 4. Clusterin is encompassed in the scope of cancerous angiogenesis-related diseases and would inherently be targeted since both applications teach the same antisense sequence and target sequence, as well as methods of delivery.

Thus in the absence of evidence to the contrary, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amy H. Bowman whose telephone number is 571-272-0755. The examiner can normally be reached on Mon-Fri 7:30 am – 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on 571-272-0811. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Patent applicants with problems or questions regarding electronic images that can be viewed in the Patent Application Information Retrieval system (PAIR) can now contact the USPTO's Patent Electronic Business Center (Patent EBC) for assistance. Representatives are available to answer your questions daily from 6 am to midnight (EST). The toll free number is (866) 217-9197. When calling please have your

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Amy H. Bowman
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